

TABLE A4

Summary of the Incidence of Nonneoplastic Lesions in *Ad Libitum*-Fed Male Mice in the 2-Year Gavage Study of Chloral Hydrate^a

	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
Disposition Summary				
Animals initially in study	60	60	60	60
15-Month interim evaluation	12	12	12	12
Early deaths				
Moribund		4	2	1
Natural deaths	6	7	10	3
Survivors				
Terminal sacrifice	42	37	36	44
Animals examined microscopically	60	60	60	60
15-Month Interim Evaluation				
Alimentary System				
Liver	(12)	(12)	(12)	(12)
Fatty change, focal, peripheral	2 (17%)	7 (58%)		
Fatty change, peripheral			7 (58%)	7 (58%)
Granuloma, multiple	3 (25%)			
Vacuolization cytoplasmic, centrilobular	9 (75%)	5 (42%)	6 (50%)	4 (33%)
2-Year Study				
Alimentary System				
Esophagus	(47)	(11)	(11)	(48)
Autolysis	4 (9%)		1 (9%)	
Polyarteritis				1 (2%)
Gallbladder	(43)	(10)	(10)	(44)
Autolysis	2 (5%)	4 (40%)	6 (60%)	1 (2%)
Crystals, epithelium	1 (2%)			
Cyst			1 (10%)	
Fibrosis				2 (5%)
Inflammation, chronic, serosa				1 (2%)
Intestine large, cecum	(41)	(5)	(4)	(46)
Autolysis				1 (2%)
Hyperplasia, lymphoid				1 (2%)
Polyarteritis				1 (2%)
Intestine large, colon	(41)	(5)	(4)	(46)
Autolysis				1 (2%)
Polyarteritis				1 (2%)
Intestine large, rectum	(41)	(5)	(4)	(43)
Granuloma	1 (2%)			
Polyarteritis				1 (2%)
Intestine small, duodenum	(41)	(7)	(4)	(46)
Autolysis		1 (14%)		1 (2%)
Intestine small, ileum	(42)	(5)	(5)	(46)
Autolysis				1 (2%)
Intestine small, jejunum	(42)	(5)	(4)	(46)
Autolysis				1 (2%)

^a Number of animals examined microscopically at the site and the number of animals with lesion

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	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
2-Year Study (continued)				
Alimentary System (continued)				
Liver	(48)	(48)	(47)	(48)
Autolysis	3 (6%)	2 (4%)		1 (2%)
Basophilic focus	3 (6%)	3 (6%)	1 (2%)	5 (10%)
Clear cell focus	1 (2%)	1 (2%)	3 (6%)	2 (4%)
Clear cell focus, multiple	1 (2%)	2	(4%) 1	(2%)
Congestion			1 (2%)	
Eosinophilic focus		1 (2%)	1 (2%)	1 (2%)
Fatty change, focal		1 (2%)		
Fibrosis, focal			1 (2%)	
Granuloma, multiple	1 (2%)		1 (2%)	
Hyperplasia, bile duct		1 (2%)		
Infarct		2 (4%)		2 (4%)
Infiltration cellular, lymphocytic	2 (4%)		1 (2%)	2 (4%)
Mixed cell focus		1 (2%)		
Necrosis, focal, hepatocyte			1 (2%)	
Necrosis, hepatocyte	1 (2%)	1 (2%)		
Necrosis, multifocal, hepatocyte	1 (2%)			
Regeneration, focal		1 (2%)		
Vacuolization cytoplasmic, centrilobular	2 (4%)	1 (2%)	2 (4%)	4 (8%)
Pancreas	(46)	(10)	(9)	(48)
Atrophy, acinar cell		1 (11%)		
Autolysis	4 (9%)		2 (22%)	1 (2%)
Cyst, duct		1 (10%)		
Fibrosis		1 (10%)		
Polyarteritis				1 (2%)
Salivary glands	(48)	(10)	(10)	(48)
Autolysis	5 (10%)			
Degeneration	1 (2%)			
Infiltration cellular, lymphocytic	9 (19%)	2 (20%)		10 (21%)
Stomach, forestomach	(43)	(10)	(10)	(46)
Autolysis	1 (2%)		1 (10%)	
Hyperkeratosis, focal	1 (2%)			
Hyperplasia, squamous	1 (2%)			
Stomach, glandular	(43)	(10)	(10)	(46)
Autolysis	2 (5%)	4 (40%)	5 (50%)	
Inflammation, acute, submucosa	1 (2%)			
Inflammation, chronic, focal				1 (2%)
Polyarteritis				1 (2%)
Tongue	(47)	(10)	(11)	(47)
Autolysis	4 (9%)		1 (9%)	
Polyarteritis				1 (2%)
Cardiovascular System				
Blood vessel	(48)	(11)	(11)	(48)
Autolysis, aorta	3 (6%)			

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	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
2-Year Study (continued)				
Cardiovascular System (continued)				
Heart	(48)	(11)	(11)	(48)
Autolysis	3 (6%)		1 (9%)	
Cardiomyopathy	1 (2%)			1 (2%)
Congestion			1 (9%)	
Hemorrhage, myocardium		1 (9%)		
Polyarteritis				1 (2%)
Endocrine System				
Adrenal gland, cortex	(45)	(11)	(10)	(46)
Autolysis	4 (9%)	2 (18%)	2 (20%)	1 (2%)
Cyst, unilateral	1 (2%)			1 (2%)
Cytologic alterations	1 (2%)			
Cytoplasmic alteration	4 (9%)	2 (18%)		5 (11%)
Degeneration, focal, unilateral				1 (2%)
Hyperplasia	6 (13%)		1 (10%)	4 (9%)
Hyperplasia, spindle cell	24 (53%)	7 (64%)	3 (30%)	27 (59%)
Hypertrophy	2 (4%)			
Adrenal gland, medulla	(45)	(11)	(10)	(45)
Autolysis	3 (7%)		1 (10%)	1 (2%)
Hyperplasia				1 (2%)
Parathyroid gland	(47)	(6)	(6)	(42)
Autolysis	4 (9%)		1 (17%)	
Cyst	1 (2%)			
Pituitary gland	(42)	(10)	(9)	(46)
Autolysis	3 (7%)	2 (20%)	1 (11%)	1 (2%)
Cyst	2 (5%)			1 (2%)
Hyperplasia, focal, pars distalis	1 (2%)			
Thyroid gland	(47)	(11)	(10)	(48)
Autolysis	4 (9%)		3 (30%)	
Cyst, follicle	5 (11%)	1 (9%)		3 (6%)
Polyarteritis				1 (2%)
General Body System				
None				
Genital System				
Coagulating gland	(46)	(10)	(10)	(48)
Autolysis	3 (7%)	1 (10%)	2 (20%)	
Distended			1 (10%)	1 (2%)
Inflammation, chronic active			1 (10%)	
Epididymis	(46)	(10)	(11)	(48)
Autolysis	3 (7%)	1 (10%)	2 (18%)	1 (2%)
Granuloma sperm	1 (2%)			2 (4%)
Granuloma, unilateral				1 (2%)
Infiltration cellular, lymphocytic				1 (2%)
Inflammation, chronic active			1 (9%)	
Inflammation, chronic	1 (2%)			
Polyarteritis				1 (2%)

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	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
2-Year Study (continued)				
Genital System (continued)				
Penis			(1)	
Concretion				1 (100%)
Inflammation, acute				1 (100%)
Preputial gland	(46)	(10) (11)	(48)	
Abscess		1 (10%)		
Atrophy	15 (33%)	4 (40%)	6 (55%) 21	(44%)
Autolysis	3 (7%)		1 (9%)	
Cyst	1 (2%)		1 (9%)	3 (6%)
Dilatation	1 (2%)			1 (2%)
Ectasia, duct		2 (20%)	5 (45%)	2 (4%)
Inflammation, acute, unilateral				1 (2%)
Inflammation, chronic, unilateral	1 (2%)			
Inflammation	1 (2%)			
Prostate	(46)	(10)	(11)	(48)
Atrophy	2 (4%)			3 (6%)
Autolysis	3 (7%)		3 (27%)	
Congestion			1 (9%)	
Ectasia, focal			1 (9%)	
Inflammation, acute				1 (2%)
Inflammation, focal				1 (2%)
Polyarteritis				1 (2%)
Seminal vesicle	(46)	(11)	(14)	(48)
Atrophy	1 (2%)			2 (4%)
Autolysis	3 (7%)	1 (9%)	2 (14%)	1 (2%)
Depletion			1 (7%)	
Dilatation	1 (2%)			1 (2%)
Distended		1 (9%)	3 (21%)	
Inflammation, chronic active			1 (7%)	
Inflammation, chronic				1 (2%)
Polyarteritis, unilateral				1 (2%)
Testes	(45)	(11)	(10)	(48)
Atrophy, unilateral	1 (2%)			
Autolysis	3 (7%)	1 (9%)	3 (30%)	1 (2%)
Degeneration, bilateral	1 (2%)			
Hyperplasia, unilateral, interstitial cell				1 (2%)
Hematopoietic System				
Bone marrow	(47)	(10)	(10)	(48)
Autolysis	3 (6%)			
Hyperplasia	1 (2%)	2 (20%)	2 (20%)	4 (8%)
Lymph node	(48)	(15)	(17)	(48)
Granuloma, inguinal	1 (2%)			
Lymph node, mandibular	(48)	(10)	(9)	(45)
Autolysis	4 (8%)			
Hyperplasia				1 (2%)
Inflammation, chronic		1 (10%)		

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2-Year Study (continued)				
Hematopoietic System (continued)				
Lymph node, mesenteric	(47)	(13)	(16)	(48)
Angiectasis, focal			1 (6%)	
Autolysis	5 (11%)			
Congestion			1 (6%)	1 (2%)
Degeneration	4 (9%)	4 (31%)	5 (31%)	5 (10%)
Granuloma			1 (6%)	
Hematopoietic cell proliferation	1 (2%)			
Hemorrhage	1 (2%)			1 (2%)
Hyperplasia	1 (2%)		1 (6%)	4 (8%)
Polyarteritis, artery				1 (2%)
Spleen	(47)	(16)	(17)	(48)
Angiectasis, focal			1 (6%)	
Apoptosis, lymphocyte		1 (6%)		
Atrophy, lymphocyte		3 (19%)	1 (6%)	2 (4%)
Autolysis	4 (9%)		2 (12%)	
Congestion		1 (6%)		
Hematopoietic cell proliferation	2 (4%)	7 (44%)	2 (12%)	7 (15%)
Hyperplasia, lymphoid	3 (6%)		3 (18%)	1 (2%)
Thymus	(29)	(6)	(4)	(35)
Autolysis	3 (10%)			1 (3%)
Ectopic parathyroid gland		1 (17%)		
Integumentary System				
Mammary gland	(5)		(2)	
Autolysis	2 (40%)			
Skin	(48)	(10)	(10)	(48)
Autolysis	4 (8%)		1 (10%)	
Granuloma	1 (2%)			
Musculoskeletal System				
Bone, femur	(46)	(11)	(12)	(48)
Autolysis	3 (7%)			
Bone, sternum	(47)	(11)	(12)	(48)
Autolysis	3 (6%)			
Fibrous osteodystrophy	4 (9%)			2 (4%)
Polyarteritis				1 (2%)
Skeletal muscle	(47)	(10)	(11)	(48)
Autolysis	4 (9%)		1 (9%)	
Infiltration cellular, lymphocytic				1 (2%)
Mineralization, focal	1 (2%)			
Polyarteritis				2 (4%)
Nervous System				
Brain, cerebellum	(47)	(10)	(9)	(48)
Autolysis	4 (9%)	1 (10%)		1 (2%)
Brain, cerebrum	(47)	(10)	(9)	(48)
Autolysis	4 (9%)	1 (10%)		1 (2%)
Hydrocephalus				1 (2%)
Mineralization, thalamus	25 (53%)	2 (20%)	1 (11%)	14(29%)

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	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
2-Year Study (continued)				
Nervous System (continued)				
Peripheral nerve	(47)	(10)	(11)	(48)
Autolysis	4 (9%)		1 (9%)	
Degeneration	2 (4%)			1 (2%)
Demyelination	1 (2%)			
Infiltration cellular, lymphocytic	1 (2%)			
Spinal cord	(47)	(10)	(9)	(48)
Autolysis	4 (9%)	1 (10%)		1 (2%)
Respiratory System				
Larynx	(46)	(11)	(11)	(47)
Autolysis	4 (9%)		1 (9%)	
Polyarteritis				1 (2%)
Lung	(48)	(20)	(16)	(48)
Atelectasis			1 (6%)	
Autolysis	3 (6%)		1 (6%)	
Congestion			1 (6%)	
Dilatation, bronchiole, glands	1 (2%)			1 (2%)
Hemorrhage, focal, alveolus			1 (6%)	
Hyperplasia, alveolar epithelium				2 (4%)
Infiltration cellular, lymphocytic	4 (8%)	1 (5%)		2 (4%)
Inflammation, chronic active		1 (5%)		
Polyarteritis				1 (2%)
Nose	(47)	(11)	(12)	(48)
Autolysis	4 (9%)		1 (8%)	
Trachea	(47)	(10)	(11)	(48)
Autolysis	4 (9%)		1 (9%)	
Dilatation, glands	1 (2%)			
Special Senses System				
Eye	(46)	(11)	(11)	(48)
Autolysis	3 (7%)		2 (18%)	
Cataract, lens		1 (9%)		
Polyarteritis				1 (2%)
Harderian gland	(47)	(16)	(12)	(47)
Atrophy, focal, unilateral	1 (2%)			
Autolysis	4 (9%)		1 (8%)	
Hyperplasia, diffuse, unilateral				1 (2%)
Hyperplasia, focal, bilateral				1 (2%)
Hyperplasia, focal, unilateral	1 (2%)			1 (2%)
Hyperplasia, unilateral	1 (2%)			1 (2%)
Hyperplasia, papillary, unilateral				1 (2%)
Infiltration cellular, lymphocytic	5 (11%)	1 (6%)	2 (17%)	
Lacrimal gland	(47)	(10)	(10)	(46)
Atrophy, focal	1 (2%)			
Autolysis	5 (11%)			
Cytoplasmic alteration				1 (2%)
Infiltration cellular, lymphocytic				2 (4%)
Zymbal's gland	(45)	(9)	(7)	(48)
Autolysis	2 (4%)			

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	Vehicle Control	25 mg/kg	50 mg/kg	100 mg/kg
2-Year Study (continued)				
Urinary System				
Kidney	(46)	(10)	(10)	(48)
Accumulation hyaline droplet, renal tubule		2 (20%)		
Angiectasis				1 (2%)
Autolysis	5 (11%)	1 (10%)	4 (40%)	1 (2%)
Congestion			1 (10%)	
Cyst, renal tubule	5 (11%)			3 (6%)
Degeneration, renal tubule	5 (11%)			3 (6%)
Glomerulosclerosis	2 (4%)	4 (40%)	1 (10%)	10 (21%)
Hydronephrosis			2 (20%)	
Infarct, unilateral	2 (4%)	1 (10%)		1 (2%)
Infiltration cellular, lymphocytic			1 (10%) 3	(6%)
Inflammation, chronic	1 (2%)			
Mineralization, renal tubule	4 (9%)	1 (10%)		3 (6%)
Nephropathy	6 (13%)		1 (10%)	3 (6%)
Regeneration, renal tubule	11 (24%)			7 (15%)
Vacuolization cytoplasmic, bilateral, renal tubule	1 (2%)			
Urinary bladder	(46)	(10)	(11)	(48)
Autolysis	3 (7%)		3 (9%)	
Infiltration cellular, lymphocytic	4 (9%)			
Inflammation, acute				1 (2%)